

DIFFERENTIAL EFFECTS OF NICOTINE ON CARDIAC NORADRENALINE
AND NEUROPEPTIDE Y RELEASE IN NORMOXIA AND ANOXIA

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Harmful cardiovascular actions of cigarette smoking have been attributed to a sympathetic activation of the heart. Hence, the effect of nicotine on cardiac release of noradrenaline, dihydroxyphenylethyleneglycol (DOPEG) and neuropeptide Y was investigated in isolated perfused guinea pig hearts. Neuropeptide Y is a sympathetic peptide transmitter, which is co-stored with noradrenaline. Common release of noradrenaline and neuropeptide Y is known to specify an exocytotic release mechanism (Arch Pharmacol 340: 509, 1989). Overflow of DOPEG, the major intraneuronal metabolite of noradrenaline, indicates a rise of free intracellular noradrenaline concentrations, which characterizes nonexocytotic noradrenaline release (Circ Res 60: 194, 1987). The latter release mechanism is not accompanied by neuropeptide Y overflow. Noradrenaline and DOPEG were determined by HPLC, neuropeptide Y was measured by radioimmunoassay.

In normoxia, nicotine (10-1000 μ M) induced a concentration dependent release of both noradrenaline and neuropeptide Y (IC₅₀: 30 μ M). The release of noradrenaline and neuropeptide Y was positively correlated ($r=0.81$) with a molar ratio of about 1000/1. The release of both transmitters was dependent on extracellular calcium and underwent rapid tachyphylaxis. No DOPEG overflow was detectable during nicotine administration in normoxia.

During energy depletion by anoxia or cyanide intoxication and glucose-free perfusion, spontaneous noradrenaline overflow occurred after 15 min and reached peak levels after 40 min (160 pmol/g/min). In presence of low nicotine concentrations (3 μ M) anoxic noradrenaline release started after 10 min with rapid increase at 20 min (250 pmol/g/min). In these experiments noradrenaline release was independent of extracellular calcium and did not coincide with neuropeptide Y release. Nicotine was present from the beginning to the end of anoxia without arising tachyphylaxis. In cyanide intoxication noradrenaline release was preceded and accompanied by DOPEG overflow. Nicotine (3 μ M) caused an acceleration of both noradrenaline and DOPEG overflow.

Summary: In normoxia, nicotine induces exocytotic release of noradrenaline and neuropeptide Y. In anoxia, nicotine accelerates anoxic noradrenaline release at concentrations, which are ineffective in normoxia, by a nonexocytotic mechanism.